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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,669	12/21/2001	Rama Akella	SBI-111	1708

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,669	AKELLA ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *32,35 and 36* is/are allowed.

6)☒ Claim(s) *1-19,23-31,and 33* is/are rejected.

7)☒ Claim(s) *20-22 and 34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Claims 33 and 34 are objected to because of the following informalities: At claim 33, line 3, and claim 34, line 3, the beginning parenthesis before "Asp" is unmatched and should be deleted. Appropriate correction is required.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no original disclosure supporting the upper limit of 25 mole % recited at claim 33, line 4. The range as disclosed in the instant application and the two parent applications is "about 10-15 mole % hydroxy amino acids". See, e.g., page 6, lines 28-29, of the instant specification.

3. The effective filing date of instant claims 1-31 and 33 is deemed to be December 21, 2001, the filing date of the instant application. Instant claims 1-31 and 33 are not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent application 09/748,038 because the parent application, under the test of 35 U.S.C. 112, first paragraph, does not disclose the genus of TGF-β superfamily polypeptides; does not disclose vinyl pyrrolidone polymers in general; does not disclose the molecular weight range of about 2.5 kD to about 20 kD; does not disclose water or aqueous buffer solutions as solvents for the growth factor composition; does not disclose the polymer concentration range of about 0.1% w/v to about 70% w/v or the narrower ranges of instant claims 8-10; does not disclose the viscosity ranges recited in instant

claims 26-29; does not disclose promoting soft tissue regeneration in general; does not disclose increasing the bioavailability of growth factors; and does not disclose a hydroxy amino acid content of a mixture of bone-derived growth factors ranging up to about 25 mole %. Accordingly, U.S. Patent Application Publication 2002/0040004, which was published based upon parent application 09/748,038 and has a different inventorship than the instant application, is available as prior art against the instant claims under 35 U.S.C. 102(e).

The effective filing date of instant claims 32, 34, and 36 is deemed to be October 16, 1998, the filing date of grandparent application 09/173,989. These claims are deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of the '989 application because the '989 application, under the test of 35 U.S.C. 112, first paragraph, discloses the claimed invention.

The effective filing date of instant claim 35 is deemed to be December 22, 2000, the filing date of parent application 09/748,038. Claim 35 is not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of grandparent application 09/173,989 because the '989 application, under the test of 35 U.S.C. 112, first paragraph, does not disclose a bone-derived growth factor mixture wherein about 60% of the protein content is histones, ribosomes, and growth factors.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1-19 and 23-31 are rejected under 35 U.S.C. 103(a) as being obvious over the Mueller et al article (Swiss Med. Wkly., Vol. 131, pages 23-25). The Mueller et al article teaches a bone protein mixture, which includes angiogenic factors such as FGF and TGF-β, in

combination with a 5% solution of povidone. The composition is injected into the myocardial tissue of pigs and results in angiogenesis. See, e.g., the Abstract and page 24, column 1, first paragraph. Because the Mueller et al article does not specify a solvent for the 5% povidone solution used therein, the solvent inherently will be either water or an aqueous buffer solution. The Mueller et al article's source of bone proteins, Provasc from Sulzer Carbomedics, is the same as Applicants' disclosed source of growth factor (see page 17, line 16), and the Mueller et al article discloses its Provasc to comprise a mixture of angiogenic factors. In view of the similarity in source and composition between the Mueller et al article's source of bone proteins and Applicants' disclosed and claimed growth factor mixtures, the two are deemed to be the same and the Mueller et al article's source of bone proteins is deemed inherently to comprise the same mixture of growth factors claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the Mueller et al article's source of bone proteins and Applicants' claimed mixture of growth factors to shift the burden to Applicants to provide evidence that their claimed mixture of growth factors is unobviously different than the Mueller et al article's source of bone proteins. The Mueller et al article does not teach a molecular weight for the povidone, does not teach povidone concentrations range from about 0.5% w/v to about 2.5% w/v, does not teach administering the composition to human patients in need of angiogenesis, and does not teach a viscosity for the povidone solutions. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal molecular weights and concentrations for the povidone solutions of the Mueller et al article, because molecular weight and concentration are art-recognized result-effective variables which are routinely determined and optimized in the polymer and pharmaceutical arts. Such a

determination would at the same time result in an optimization of the viscosity of the polymer-containing solution. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the compositions of the Mueller et al article to induce angiogenesis in ischemic myocardial tissue in human patients because it is desirable to induce angiogenesis in such patients so as to restore blood flow to the injured organ, and because the pig subjects of the Mueller et al article are in vivo models which are reasonably predictive of success in human patients. With respect to instant claim 30, myocardial and heart tissue are soft tissues. With respect to instant claim 31, the Mueller et al article adds bone protein to the solvent containing povidone rather than adds povidone to the solvent containing povidone. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to add the bone protein and povidone of Mueller et al to the solvent in any order because the order of adding solutes to the solvent would not have been expected to have any effect on the properties of the resulting solution, and because changes in the sequence of adding ingredients are prima facie obvious. See MPEP 2144.04(IV)(C).

6. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being obvious over the Chemical Abstract 132:40522x. The Chemical Abstract 132:40522x teaches forming an aqueous solution of bone morphogenetic protein and combining it with a second aqueous solution of bFGF and PVP. The resultant composition is used for osteogenesis stimulation. Because the same growth factor, solvent, and vinyl pyrrolidone polymer are combined according to the same method steps in the Chemical Abstract as in Applicants' claimed invention, inherently the bioavailability of the BMP in the Chemical Abstract will be increased to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the method of the Chemical

Abstract and Applicants' claimed method to shift the burden to Applicants to show that the claimed method is unobviously different than that of the Chemical Abstract. The Chemical Abstract 132:40522x does not teach a molecular weight or solution concentration for its PVP. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine a molecular weight and solution concentration for the PVP of the Chemical Abstract because molecular weight and solution concentration are art-recognized result-effective variables which are routinely determined and optimized in the polymer, solution chemistry, and pharmaceutical arts. The Chemical Abstract 132:40522x does not teach Applicants' claimed intended use limitation. However, prima facie obviousness is not rebutted by merely recognizing additional advantages or latent properties present in the prior art. See MPEP 2145(II) and especially In re Dillon, 16 USPQ2d 1897 (Fed. Cir. 1990). There is no reason to expect that the ability of the composition to promote angiogenesis is due to the particular molecular weight of the PVP.

7. Applicant's arguments filed September 29, 2003 have been fully considered but they are not persuasive.

The obviousness rejection based upon the Mueller et al article (Swiss Med. Wkly., Vol. 131, pages 23-25) is maintained. The Mueller et al article is available as prior art against the rejected claims under 35 U.S.C. 102(a). Applicants' arguments do not satisfy the requirements for a declaration under 37 CFR 1.131, and do not satisfy the requirements for showing derivation under 37 CFR 1.132.

The obviousness rejection based upon the Chemical Abstract 132:40522x is maintained. As noted above, the Abstract does not teach Applicants' intended use limitation. However, there

is no reason to believe that the claimed composition's ability to promote angiogenesis is due to the molecular weight of the vinyl pyrrolidone polymer, i.e. is due to the single difference between the claimed composition and the prior art composition. There is no evidence that the prior art composition does not itself possess the ability to promote angiogenesis. See Dillon. Accordingly, when evidence of obviousness is weighed against the evidence of non-obviousness, the former is deemed to preponderate.

8. Claims 20-22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 32, 35, and 36 are allowed. Claim 33 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, first paragraph, and the claim objection set forth in this Office action. Claim 34 would be allowable if rewritten or amended to overcome the claim objection set forth in this Office action.

9. References crossed off of the Information Disclosure Statement filed October 22, 2003 are duplicate citations.

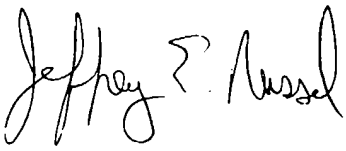
10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

November 13, 2003